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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/552,087	04/21/2000	Joseph R. Byrum	16517.132/38-21 (15786)B	4196

7590 09/15/2006

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ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 09/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/552,087	BYRUM, JOSEPH R.	
	Examiner	Art Unit	
	Juliet C. Switzer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 7/6/06.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 3,5-7,9,10 and 12-20 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 3,5-7,9,10 and 12-20 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is written in response to applicant's correspondence received 7/6/06 . Claims 3, 7, 12-16 and 20. Claims 3, 5-7, 9, 10 and 12-20 are pending. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. **This action is FINAL.**

Priority

2. Instant SEQ ID NO: 1 was disclosed as SEQ ID NO: 141338 in application 09/521640 and as SEQ ID NO: 5 in application 09/421106, therefore the instant claims are granted priority to at least 10/15/99. The presence of the sequence in the provisional application was not determined as there was no intervening reference, and as there are thousands of sequences in the provisional application and there is no reasonable way to search the application.

Claims Interpretation

3. Regarding the scope of claims 3, 5, 6, 7, 9, and 10, the remand by the board suggests three possible interpretations (see p. 8 of the remand). It is clear from the plain language of the claim that the "promoter region" of the nucleic acid molecule within the cell must comprise SEQ ID NO: 1, but the claim does not set forth any functional language to describe what SEQ ID NO: 1 is doing within this promoter region. Thus, the Board suggests that the claim can be interpreted such that (1) SEQ ID NO: 1 contains a promoter region which does function in plant

cells to cause production of an mRNA molecule, (2) that SEQ ID NO: 1 contains a "regulatory element" that acts in concert with a promoter region, for example SEQ ID NO: 1 is an enhancer, or (3) that SEQ ID NO: 1 is merely present within the construct as a "filler" sequence between the promoter region and a structural nucleic acid, and thus is part of the "promoter region" but imparts no function thereto.

It is well settled that the claims must be given their broadest reasonable interpretation in view of the specification.

The specification discloses over twenty thousand nucleic acid molecules that were isolated from the plant species *Glycine max*. The specification teaches that each one of these molecules may comprise regulatory elements (p. 16), may comprise genes encoding polypeptides or fragments thereof (p. 24) or may comprise introns and/or intron/exon junctions (p. 29). There is no further guidance in the specification, however, to assist one in determining which of these possible characterizations is applicable to instant SEQ ID NO: 1. The specification provides only one specific reference to SEQ ID NO: 1 individually, on page 101 the specification teaches that SEQ ID NO: 1 has 50% identity to a putative POL3 protein from *A. thaliana*. The specification does not, however, disclose what portion of this putative protein has identity with SEQ ID NO: 1. A sequence search by the examiner was unable to confirm this result. All other discussion in the specification of the potential function of the disclosed polynucleotide is generic in nature because it refers to all 20,082 nucleic acids disclosed in the specification in mass.

The specification teaches that the present invention includes "nucleic acid molecules having promoter regions or partial promoter regions, including those located within SEQ ID NO: 1 through SEQ ID NO: 20082 (p. 16)." Thus implying that a promoter region or a partial

promoter region may be within SEQ ID NO: 1. The specification teaches that promoters "can include between about 300bp upstream and about 10kb upstream of the trinucleotide ATG sequence at the start site of a protein coding region (p. 16, final ¶)," and that "While in many circumstances a 300bp promoter may be sufficient for expression, additional sequences may act to further regulate expression (p. 17, 1st ¶)."

The specification does not provide any specific guidance as to whether SEQ ID NO: 1 in particular comprises regulatory elements, sequence encoding polypeptides, introns, or intron/exon junctions. Given that the specification asserts that instant SEQ ID NO: 1 may include any or all of these, but fails to even positively identify a single one of these suggested elements within SEQ ID NO: 1, it cannot be definitely determined if SEQ ID NO: 1 actually contains a promoter or not, based on the teachings of the specification.

Turning to the three possible interpretations set forth by the Board of Appeals, the specification clearly supports the first possible interpretation. The specification further clearly suggests that the claimed molecules may encompass "regulatory elements" as discussed beginning on page 17 through page 24, which is the second interpretation. Regarding the third interpretation, however, the specification does not ever appear to suggest the use of SEQ ID NO: 1 or any of the disclosed nucleic acids to "serve as a filler sequence between the promoter region and a structural nucleic acid molecule," and thus this potential interpretation of the claimed invention does not appear to be applicable to the instant claims, when the claims are interpreted in light of the specification. The board's remaining comments are addressed in the rejections in this office action.

Claim Rejections - 35 USC § 101

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 3, 5-7, 9-10, and 12-20 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility.

Rejected claims 3, 5-7, and 9-10 are drawn to plant host cells and transgenic plants that comprise a construct having a promoter, wherein the promoter nucleic acid molecule comprises SEQ ID NO: 1 or a complement thereof linked to a structural nucleic acid molecule and a 3' non-translated sequence that functions in said cell to cause termination of transcription.

Claims 12-20 are drawn to substantially purified nucleic acid molecules that comprise instant SEQ ID NO: 1 or a nucleic acid sequence that is related to instant SEQ ID NO: 1 by a percent identity. Thus the claims encompass SEQ ID NO: 1 and many, many variants of the sequence.

The claimed subject matter is not supported by a specific, substantial, and credible utility because the disclosed uses are generally applicable to broad classes of this subject matter. In addition, further characterization of the claimed subject matter would be required to identify or reasonably confirm a "real world" use.

A well-established utility is defined as a specific, substantial and credible utility which is well known, immediately apparent or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. The instant host cells and transgenic plants do not have a well established utility because the art does not teach any

utility for the instantly claimed host cells and transgenic plants that is specific, substantial, and credible.

The specification discloses a number of general utilities for the nucleic acids disclosed herein. For example, the specification generally discloses that these nucleic acids are useful in genetic mapping studies (p. 35), physical mapping (p. 43), contig mapping (p. 46), comparative mapping (p. 49-56), the identification of polymorphisms (p. 49-56), monitoring expression (p. 56), locating regions of identity by descent between individuals (p. 58), isolating clones (p. 59), microarray based methods (p. 60), direct site mutagenesis (p. 60), transformation (p. 62-80), in cosuppression (p. 80), to reduce gene function (p. 82), and as antibodies (p. 83). None of these asserted utilities are specific because the disclosed uses of the nucleic acids are generally applicable to any nucleic acid and therefore are not particular to the nucleic acid sequences being claimed.

The instant specification herein discusses transformation of cells and plants in general (p. 62-80), but does not discuss these methodologies with regard to SEQ ID NO: 1 in particular. The specification in table 1 sets forth that the protein encoded by instant SEQ ID NO: 1 has 50% identity with a putative POL3 protein from Arabidopsis, but the specification does not assert a utility for SEQ ID NO: 1 or the protein encoded by SEQ ID NO: 1 based on this homology. The fact that SEQ ID NO: 1 encodes a polypeptide that has homology to a "putative" protein suggests that the functionality of the Arabidopsis protein has not been confirmed. Thus, further experimentation would be required to reasonably confirm the identity of the protein both for Arabidopsis and for Glycine max proteins. Beyond that, further experimentation would still be required to establish a real world utility for such a protein.

The specification teaches that nucleic acid molecules and fragments thereof may be employed as genetic markers (p. 35 and following). Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities, and this is particularly the case with regard to correlation with phenotypic traits or genetic mapping of phenotypic traits. The specification has not demonstrated that instant SEQ ID NO: 1 is related to any particular phenotypic trait, nor has it provided any specific suggestion or discussion of any trait SEQ ID NO: 1 might be related to.

The specification suggests that the claimed nucleic acids may be used in transformation to express any polypeptide that is encoded by the transformed sequence (p. 62 and following). No specific function of the polypeptide encoded by SEQ ID NO: 1 has been provided. The specification has provided no information as to what effect the expression of SEQ ID NO: 1 in a transgenic plant cell or plant would have on the plant. The suggestion that instant SEQ ID NO: 1 can be used to transform plants is an invitation to do further research to determine what effect the sequence might have on plants, or what product is produced upon expression of the encoded polypeptide, if one is encoded.

Claims 3, 5-6, 7, 9, and 10, are drawn to transformed plant cells and transgenic plants that have a construct which contains instant SEQ ID NO: 1 or its complement as "an exogenous promoter region" that functions in a plant cell to cause the production of an mRNA molecule. Thus, these claims suggest that SEQ ID NO: 1 is being included in the host cells and transgenic plants of claim 3, 5, and 6 for its functionality as a "promoter." This is not considered a substantial utility because further experimentation would be required to reasonably confirm that

SEQ ID NO: 1, or its complement, or fragments of either would function as a promoter as required by the claims.

The specification does not provide any guidance as to the use of SEQ ID NO: 1, its complement or fragments thereof as promoters. In order to use the claimed invention, one would first have to confirm that either SEQ ID NO: 1 or its complement is in fact a promoter, then determine which fragments are also promoters. There is no evidence on the record to point one to the conclusion that the instantly disclosed sequence is or contains a promoter rather than an intron or a coding sequence, both of which are also suggested as possibilities for SEQ ID NO: 1. The specification teaches at page 101 that instant SEQ ID NO: 1 has 50% identity with a gene encoding a putative POL3 protein from Arabidopsis thaliana. The examiner was not able to confirm this result with a sequence search. However, a sequence search did reveal a sequence disclosed post-filing of this application that has 40.5% with instant SEQ ID NO: 1 identity to a POL3-like gene from *Phaseolus coccineus*, and that this identity occurs over a portion of the gene that is within the portion encoding the translated protein (see attached alignment and further explanation). The sequence search did not identify any sequences with which instant SEQ ID NO: 1 had identity to any promoter.

Even if one were to assume that SEQ ID NO: 1 contained or was a "promoter," one would have to determine the type of promotion conferred by SEQ ID NO: 1, that is, one would have to determine if the promotion is tissue specific or constitutive, for example, or if it is an inducible promoter, and under what circumstances it is induced or repressed in order to make use of the claimed host cells or plants. Without knowing the conditions under which the promoter could be used one would not know how to use the invention. Each of these determinations is

highly unpredictable, from the determination as to whether or not SEQ ID NO: 1 or its complement is in fact a promoter to the determination of the type of promoter it may be to the determination of fragments of the promoter that confer promotion activity. There has been no specific assertion that in fact SEQ ID NO: 1 is a promoter, aside from the claims. The specification generally suggests that all of the sequences disclosed in the application might be promoter molecules (p. 16), but the specification also generally suggests that all of these molecules may comprise introns and coding sequences (p. 24 and 29). Thus, the teachings of the specification themselves, by providing a number of different potential and conflicting descriptions of SEQ ID NO: 1 provide reason to question whether the sequence in fact comprises a promoter, a partial promoter, an exon or an intron or some combination of these. The specification has not provided any further guidance as to the use of SEQ ID NO: 1 as a promoter or its use in any other capacity. Thus, it is left to one attempting to make and use the claimed products to determine which instant SEQ ID NO: 1 actually is and how it can be used within the constructs claimed. Even given the choice between the suggestion that SEQ ID NO: 1 comprises a promoter or a partial promoter, the specification does not provide any guidance or suggestion as to which is the case for SEQ ID NO: 1. This is an important distinction since the entire functioning of a promoter is entirely sequence specific. For example, if SEQ ID NO: 1 contained only a partial promoter, it is highly unpredictable as to whether or not that partial promoter would function to promote production of an mRNA or which part of SEQ ID NO: 1 is in fact the "promoting" part since one cannot simply look at SEQ ID NO: 1 and identify these regions by any disclosed sequence characteristics, and since the function of a promoter is highly sequence specific. Or, if SEQ ID NO: 1 contains a regulatory element, it is highly unpredictable how that

element would function in view of the fact that there are hundreds of possible regulatory functions known, and there is no known way to predict if one of these is attributable to instant SEQ ID NO: 1. The instant specification provides a seven page listing of possible functions that any potential regulatory element contained within the disclosed sequences might have (pages 17-23). Each function would warrant use in a different type of system for expression under different circumstances to achieve an effect specific to the regulatory element. For example, the specification makes reference to oxygen responsive elements, light regulatory elements, and elements responsive to gibberellin. In order to make the claimed invention, one would have to undertake enormous amounts of experimentation to discover if in fact SEQ ID NO: 1 is a promoter or comprises a promoter or a regulatory element, as suggested by the claims and also suggested by the specification, or if SEQ ID NO: 1 contains a structural gene as also suggested by the specification, or if SEQ ID NO: 1 comprises an intron or an intron/exon boundary as also suggested by the specification.

Considering then, the state of the prior art, instant SEQ ID NO: 1 is a novel sequence. A sequence search by the examiner in a variety of nucleic acid databases did not identify any sequence in the prior art with greater than 29% identity over the full length of SEQ ID NO: 1. For example, GenBank AF147259 (13 August 1999) provides the sequence of an A. thaliana BAC, and nucleotides 46185-46519 of this sequence have 29% identity with instant SEQ ID NO: 1. This however is an uncharacterized portion of nucleic acid, and even if the homology were exact would not provide any further guidance as to whether instant SEQ ID NO: 1 contains a promoter or promoter elements, or an intron, or a coding sequence.

Given all of these considerations, the use of instant SEQ ID NO: 1 as a promoter is not a specific or substantial utility since further experimentation would be required to confirm that in fact SEQ ID NO: 1 has the ability to cause the production of an mRNA molecule and the conditions under which such activity occurs. Thus, no utility has been described for the transformed plant cells and transgenic plants comprising SEQ ID NO: 1 wherein SEQ ID NO: 1 is within the construct as a promoter.

It has not been demonstrated that SEQ ID NO: 1 has any utility as a marker for a specific phenotypic trait. After further research, a specific and substantial credible utility might be found for the claimed cells and plants. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's invention is incomplete.

In the instant case, the specification has provided a wide variety of general guidance that any of the over twenty thousand disclosed sequences may be promoters, coding sequences or introns. The specification has suggested that any of these may be useful for a wide variety of purposes, some of which conflict with one another. For example, if SEQ ID NO: 1 is a promoter or contains a promoter, it is not a coding portion of a gene. If SEQ ID NO: 1 is a promoter, than it would not be an expressed sequence so it could not be used to monitor expression of genes via a microarray (as suggested on page 56). The instant claims are limited to instant SEQ ID NO: 1, and some of these require that SEQ ID NO: 1 is within an exogenous promoter region. However, these claims do not remove the entirely general disclosure of the specification which suggests a wide variety of functions and uses for all of the disclosed sequences, but no specific and substantial utility for any one sequence, including instant SEQ ID NO: 1.

The facts in this case are very similar to the facts in In re Fisher (CAFC, 04-1465, 9/7/2005). In both applications, a general disclosure is given to support the disclosure of a nucleic acid whose particular function is not disclosed. The court found that none of the utilities generally suggested for the claimed nucleic acids and compositions in the Fisher case (as a molecular marker, measuring expression, source for primers, identifying polymorphisms, isolating primers, controlling protein expression, or searching for genes in other plants) was enough to overcome the utility requirement. The instant case is similar in that the specification provides merely hypothetical possibilities for uses for the claimed invention. The court has ruled that these are not sufficient to provide a specific and substantital utility to the claimed invention.

As noted by Brenner v. Manson, 383 U.S. 519, 535-536 (1996), and quoted in In re Fisher, "Congress intended that no patents be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing...a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." Neither the specification as filed nor any art of record discloses or suggests any property or activity for the claimed cells and plants such that another non-asserted utility would be well established for the compounds.

For these reasons, the claimed nucleic acids, host cells and transgenic plants are not supported by either a specific and substantial asserted utility or a well established utility. Note, because the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth above, credibility has not been assessed.

Claim Rejections - 35 USC § 112, 1st paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3, 5-7, 9-10, and 12-20 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

For all the above reasons, the disclosure is insufficient to teach one of skill in the art how to use the invention. A review of *In re Wands,* 8 USPQ2d 1400 (CAFC 1988) clearly points out the factors to be considered in determining whether a disclosure would require undue experimentation and include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. All of these factors are considerations when determining the whether undue experimentation would be required to use the claimed invention. As is evidenced in the discussions *supra*, each of these factors have been carefully considered in the instant grounds of rejection, and it is maintained that undue experimentation would be required by the skilled artisan to use the instant invention.

Claim Rejections - 35 USC § 112

6. Claims 3, 5, 6, 7, 9, 12, 13, 14, 15, 16, 17, 18, 19, and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain

subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Independent claim 3 is drawn to a transformed plant cell having a nucleic acid molecule which comprises "(A) an exogenous promoter region which functions in said cell to cause the production of a mRNA molecule, wherein said promoter nucleic acid molecule comprises SEQ ID NO: 1 or a complement thereof", wherein (A) is linked to a structural nucleic acid molecule encoding a polypeptide or protein and a 3' non-translated sequence that functions in said cell. Dependent claims 5 and 6 merely recite that the plant cell is a monocot or dicot plant cell. Thus, the nature of the invention in this case is that the claimed invention is to a plant cell comprising an exogenous promoter- and that promoter comprises therein SEQ ID NO: 1.

Independent claim 7 is drawn to a transformed plant having a nucleic acid molecule which comprises "(A) an exogenous promoter region which functions in said cell to cause the production of a mRNA molecule, wherein said promoter nucleic acid molecule comprises SEQ ID NO: 1 or a complement thereof", wherein (A) is linked to a structural nucleic acid molecule encoding a polypeptide or protein and a 3' non-translated sequence that functions in said cell. Dependent claims 9 and 10 merely recite that the plant cell is a monocot or dicot plant cell. Thus, the nature of the invention in this case is that the claimed invention is to a plant cell comprising an exogenous promoter- and that promoter comprises therein SEQ ID NO: 1.

Regarding the scope of the claims, the remand by the board suggests three possible interpretations (see p. 8 of the remand). It is clear from the plain language of the claim that the "promoter region" of the nucleic acid molecule within the cell must comprise SEQ ID NO: 1, but

the claim does not set forth any functional language to describe what SEQ ID NO: 1 is doing within this promoter region. Thus, the Board suggests that the claim can be interpreted such that (1) SEQ ID NO: 1 contains a promoter region which does function in plant cells to cause production of an mRNA molecule, (2) that SEQ ID NO: 1 contains a "regulatory element" that acts in concert with a promoter region, for example SEQ ID NO: 1 is an enhancer, or (3) that SEQ ID NO: 1 is merely present within the construct as a "filler" sequence between the promoter region and a structural nucleic acid, and thus is part of the "promoter region" but imparts no function thereto.

The rejected claims also include claims 12-20 which are drawn to substantially purified nucleic acid molecules which comprise or consist of SEQ ID NO: 1 or a nucleic acid molecule that has a particular percent identity with SEQ ID NO: 1 (as little as 70% identity, with some claims requiring 100% identity).

The specification discloses over twenty thousand nucleic acid molecules that were isolated from the plant species *Glycine max*. The specification teaches that each one of these molecules may comprise regulatory elements (p. 16), may comprise genes encoding polypeptides or fragments thereof (p. 24) or may comprise introns and/or intron/exon junctions (p. 29). There is no further guidance in the specification, however, to assist one in determining which of these possible characterizations is applicable to instant SEQ ID NO: 1. The specification provides only one specific reference to SEQ ID NO: 1 individually, on page 101 the specification teaches that SEQ ID NO: 1 has 50% identity to a putative POL3 protein from *A. thaliana*. The specification does not, however, disclose what portion of this putative protein has identity with SEQ ID NO: 1. A sequence search by the examiner was unable to confirm this result. All other

discussion in the specification of the potential function of the disclosed polynucleotide is generic in nature because it refers to all 20,082 nucleic acids disclosed in the specification in mass.

The specification teaches that the present invention includes "nucleic acid molecules having promoter regions or partial promoter regions, including those located within SEQ ID NO: 1 through SEQ ID NO: 20082 (p. 16)." Thus implying that a promoter region or a partial promoter region may be within SEQ ID NO: 1. The specification teaches that promoters "can include between about 300bp upstream and about 10kb upstream of the trinucleotide ATG sequence at the start site of a protein coding region (p. 16, final ¶)," and that "While in many circumstances a 300bp promoter may be sufficient for expression, additional sequences may act to further regulate expression (p. 17, 1st ¶)."

The specification does not provide any specific guidance as to whether SEQ ID NO: 1 comprises regulatory elements, sequence encoding polypeptides, introns, or intron/exon junctions. Given that the specification asserts that instant SEQ ID NO: 1 may include any or all of these, it is highly unpredictable based on the teachings of the specification as to whether or not instant SEQ ID NO: 1 contains or is a promoter element.

Turning to the three possible interpretations set forth by the Board of Appeals, the specification clearly supports the first possible interpretation. The specification further clearly suggests that the claimed molecules may encompass "regulatory elements" as discussed beginning on page 17 through page 24, which is the second interpretation. Regarding the third interpretation, however, the specification does not ever appear to suggest the use of SEQ ID NO: 1 or any of the disclosed nucleic acids to "serve as a filler sequence between the promoter region and a structural nucleic acid molecule," and thus this potential interpretation of the claimed

invention does not appear to be applicable to the instant claims, when the claims are interpreted in light of the specification.

The specification does not exemplify the use of SEQ ID NO: 1 attached to or within a promoter construct. Regarding the potential function of SEQ ID NO: 1, the specification does not provide any specific teaching. The specification discloses over twenty thousand nucleic acid molecules that were isolated from the plant species *Glycine max*. The specification teaches that each one of these molecules may comprise regulatory elements (p. 16), may comprise genes encoding polypeptides or fragments thereof (p. 24) or may comprise introns and/or intron/exon junctions (p. 29). The specification teaches that the present invention includes "nucleic acid molecules having promoter regions or partial promoter regions, including those located within SEQ ID NO: 1 through SEQ ID NO: 20082 (p. 16)." Thus implying that a promoter region or a partial promoter region may be within SEQ ID NO: 1. However, since all assertions of the function of SEQ ID NO: 1 are given generally for this sequence and over twenty thousand other sequences, none of these statements can be considered specific to SEQ ID NO: 1. Further, the different statements conflict, as it is highly unlikely that the single 394 base pair fragment of SEQ ID NO: 1 at the same time comprises regulatory elements, structural genes, intron and promoter regions.

Thus, given the instant specification, it is highly unpredictable how to use instant SEQ ID NO: 1 as part of an exogenous promoter region as set forth in claims 1 and 7. First, while the specification suggests that SEQ ID NO: 1 may contain a promoter or a partial promoter, the specification suggests with equal specificity that SEQ ID NO: 1 may contain a structural gene encoding a protein, that SEQ ID NO: 1 may contain an intron, and that SEQ ID NO: 1 may

contain and intron/exon boundary. Thus, it is left to one attempting to make and use the claimed products to determine which instant SEQ ID NO: 1 actually is and how it can be used within the constructs claimed. Even given the choice between the suggestion that SEQ ID NO: 1 comprises a promoter or a partial promoter, the specification does not provide any guidance or suggestion as to which is the case for SEQ ID NO: 1. This is an important distinction since the entire functioning of a promoter is entirely sequence specific. For example, if SEQ ID NO: 1 contained only a partial promoter, it is highly unpredictable as to whether or not that partial promoter would function to promote production of an mRNA or which part of SEQ ID NO: 1 is in fact the "promoting" part since one cannot simply look at SEQ ID NO: 1 and identify these regions by any disclosed sequence characteristics, and since the function of a promoter is highly sequence specific. Or, if SEQ ID NO: 1 contains a regulatory element, it is highly unpredictable how that element would function in view of the fact that there are hundreds of possible regulatory functions known, and there is no known way to predict if one of these is attributable to instant SEQ ID NO: 1. For example, the instant specification provides a seven page listing of possible functions that any potential regulatory element contained within the disclosed sequences might have (specification pages 17-23). Each function would warrant use in a different type of system for expression under different circumstances to achieve an effect specific to the regulatory element. For example, the specification makes reference to oxygen responsive elements, light regulatory elements, and elements responsive to gibberellin. In order to make the claimed invention, one would have to undertake enormous amounts of experimentation to discover if in fact SEQ ID NO: 1 is a promoter or comprises a promoter or a regulatory element, as suggested by the claims and also suggested by the specification, or if SEQ ID NO: 1 contains a structural

gene as also suggested by the specification, or if SEQ ID NO: 1 comprises an intron or an intron/exon boundary as also suggested by the specification.

Considering then, the state of the prior art, instant SEQ ID NO: 1 is a novel sequence. A sequence search by the examiner in a variety of nucleic acid databases did not identify any sequence in the prior art with greater than 29% identity over the full length of SEQ ID NO: 1. For example, GenBank AF147259 (13 August 1999) provides the sequence of an A. thaliana BAC, and nucleotides 46185-46519 of this sequence have 29% identity with instant SEQ ID NO: 1. This however is an uncharacterized portion of nucleic acid, and even if the homology were exact would not provide any further guidance as to whether instant SEQ ID NO: 1 contains a promoter or promoter elements, or an intron, or a coding sequence.

Furthermore, even if SEQ ID NO: 1 contains a functioning promoter or regulatory element, with regard to claims 12-15, the prior art makes clear that the ability of a promoter to function is highly sequence specific. The art teaches repeatedly that mutations in a critical region of a promoter element can destroy the ability of a construct to function in promotion. For example, Pietrzkowski *et al.* (Experimental Cell Research, 193, 283-290 (1991)) teaches that when synthetic promoters were produced wherein the sequence of an enhancer element was mutated, little to no promotion was observed from the constructs where the promoter was mutated (see for example Figure 6). Chan *et al.* (Plant Molecular Biology 46 :131-141, (2001)) teach that mutation in a critical XXIII element of the GAPB promoter abolished transcription completely (Figure 6), while mutations in other elements did not abolish activity (Figure 6). Thus, it is evident that it is highly unpredictable how promoter elements will respond to even very minor sequences changes. In addition, the order in which promoter elements occur in a

construct has an effect on the functionality of the promoter. Omilli *et al.* (Molecular and Cellular Biology, June 1986, p. 1875-1885) teach that the relative arrangement of promoter elements is a critical factor contributing to the activity of the promoter (ABSTRACT, for example).

Thus, having considered the scope of the claims, the teaching in the specification, the guidance in the prior art, the lack of working examples, and the high level of unpredictability with respect to the prior art, it is concluded that it would require undue experimentation to make and use the claimed invention.

Claim Rejections - 35 USC § 112

7. Claims 12, 13, 14, 15, 17, 18, and 19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The analysis used in this Written Description rejection follows the guidelines provided in the Federal Register, Vol. 66, No. 4, January 1, 2001, beginning at page 1099 (referred to in the rejection as "the guidelines.").

The guidelines direct one, for each claim, to determine **what the claim as a whole covers** (p. 1105, 2nd column).

Claim 12 is drawn to a substantially purified nucleic acid molecule, wherein said nucleic acid molecule comprises a nucleotide sequence having between 100% or 70% identity with SEQ ID NO: 1, or a complement thereof. Claims 13, 14, and 15 are similar to claim 12 except they

increasingly narrow the lower end of the recited homology to 80%, 90%, and 95%, respectively. The language of the claim is sufficiently broad so as to encompass nucleic acids which comprise SEQ ID NO: 1 or which have partial identity to SEQ ID NO: 1. Such molecules with identity to SEQ ID NO: 1 encompass variants of SEQ ID NO: 1 such as allelic variants having single nucleotide or larger polymorphisms, fragments of genomic molecules that include additional intron or exon sequence, potential splice variants of SEQ ID NO: 1, for example. Because the claims do not recite any functional requirement for the claimed polynucleotide, the claims encompass molecules wherein the putative encoded polypeptide has similar functionality as that encoded by SEQ ID NO: 1, and those molecules where the functionality is different. Likewise, if SEQ ID NO: 1 is a regulatory molecule (an intron or promoter or enhancer, for example) the claims encompass molecules in which whatever regulatory function the molecule has is abolished. Claim 17 specifically recites that the nucleic acid molecule further comprises a region having a single nucleotide polymorphism. This claim could be interpreted to mean that the SNP is within SEQ ID NO: 1, or it is within a sequence that is contiguous with SEQ ID NO: 1. Claim 18 recites that the molecule further comprises a promoter or partial promoter region. This could be interpreted as meaning SEQ ID NO: 1 contains this region, or it could be interpreted as meaning the claimed molecule comprises SEQ ID NO: 1 in addition to such a region further appended. Claim 19 recites that the promoter region of claim 18 comprises a CAAT cis element and a TATA cis element, plus an additional cis element. Instant SEQ ID NO: 1 contains a CAAT at nucleotides 156-159, but does not contain a TATA. Thus, this claim expressly requires additional sequence with a TATA element and an additional element, should

SEQ ID NO: 1 not include an additional cis element. Thus, the claims encompass a wide variety of potential molecules.

Next, the guidelines direct a review of the application to understand **how the application provides support for the claimed invention**.

The specification teaches a single molecule within the scope of the claimed invention, that is SEQ ID NO: 1. The specification does not teach any variants of SEQ ID NO: 1, nor does the specification teach any single nucleotide polymorphism within SEQ ID NO: 1. Thus, the single molecule provided in the specification represents only one species within the vast genus claimed.

Considering then, the scope of the claims and the teachings of the specification, the guidelines direct one to **determine whether there is sufficient written description to inform a skilled artisan that applicant was in possession of the claimed invention as a whole** at the time the application was filed. The guidelines direct that such possession may be shown in many ways, including an actual reduction to practice, detailed drawings or in chemical formulas, and description of sufficient, relevant, identifying characteristics. In addition, for a claim drawn to a genus the requirement may be satisfied by description of a representative number of species, reduction to drawings, or by disclosure of other sufficient, relevant, identifying characteristics.

The instant specification does not provide sufficient written description to inform one of possession of the invention as a whole. There is actual reduction to practice of only a single embodiment within claims 12-15. Regarding claim 17, there is no reduction to practice as there is no region having a single nucleotide polymorphism that is taught within SEQ ID NO: 1. Regarding claims 18-19, while SEQ ID NO: 1 includes a single CAAT sequence, there is no

teaching of SEQ ID NO: 1 with a TATA element, nor is there any description of additional cis elements within SEQ ID NO: 1. Reduction to practice of only a single embodiment is not reduction to practice of the entire scope of the claim, and thus, applicant has not met the written description requirement by reduction to practice.

The only structural chemical formula given in the specification is SEQ ID NO: 1. For all of the rejected claims, only a partial structure representing the entire genus is given, that is SEQ ID NO: 1. The teachings of the specification do not couple this structure with any additional physical or chemical characteristics or functional characteristics. This structural formula represents only a single species of the claimed invention for claims 12-15 and not even a single species of the claimed invention for claims 17-19. As noted in this rejection, however, the claimed invention is quite broad in nature, and this single example is not a "representative number of species" since the entire genus of molecules encompassed within this genus is so broad and includes molecules of any possible function.

The level of skill in the art is quite high, but the unpredictability regarding the functioning of nucleic acid sequences upon modification is even higher. The function of a nucleic acid, with regard to a coding or non-coding function is highly sequence dependent. For example, the art teaches repeatedly that mutations in a critical region of a promoter element can destroy the ability of a construct to function in promotion. For example, Pietrzkowski *et al.* (Experimental Cell Research, 193, 283-290 (1991)) teaches that when synthetic promoters were produced wherein the sequence of an enhancer element was mutated, little to no promotion was observed from the constructs where the promoter was mutated (see for example Figure 6). Chan *et al.* (Plant Molecular Biology 46 :131-141, (2001)) teach that mutation in a critical XXIII

element of the GAPB promoter abolished transcription completely (Figure 6), while mutations in other elements did not abolish activity (Figure 6). Thus, it is evident that it is highly unpredictable how promoter elements will respond to even very minor sequences changes. In addition, the order that promoter elements occur in a construct has an effect on the functionality of the promoter. Omilli *et al.* (Molecular and Cellular Biology, June 1986, p. 1875-1885) teach that the relative arrangement of promoter elements is a critical factor contributing to the activity of the promoter (ABSTRACT, for example). In this case, there is no functional requirement given regarding the claimed nucleic acids, and thus the claimed nucleic acids encompass a wide variety of structurally distinct molecules whose function may or may not be associated with SEQ ID NO: 1 in the same manner.

Thus, having carefully considered all of these factors, it is concluded that the specification does not provide adequate written description for the claimed invention.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 3, 5, 6, 7, 9, and 10-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Tanksley et al. (US 5648599).

Tanksley et al teach a transformed plant cell and transformed plants comprising said cells, wherein said cells comprise an exogenous promoter, a structural gene, and a termination sequence (see the claims, for example). Regarding claims 10-20, the nucleic acids taught by Tanksley et al. comprise "a complement" of SEQ ID NO: 1. These claims are anticipated by Tanksley et al. insofar as they require only a instant SEQ ID NO: 1 or "a complement thereof." The use of the indefinite article "a" to modify the required complement is interpreted to require that the claimed molecules only have to have any portion that is "a" complement of SEQ ID NO: 1, including a single nucleotide. Thus, the molecules taught by Tanksley et al. are considered to have the constructs claimed insofar as they comprise "a complement" of SEQ ID NO: 1. Amendment of the claim to read "the complement thereof" will overcome this rejection. Tanksley et al. further teach both monocot transformed plants and dicot transformed plants (see the claims, for example).

10. Claims 10-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Stratagene Catalog (1997, p. 95).

Stratagene teaches a mix of substantially purified molecules having therein every possible hexamer sequence. Regarding claims 10-20, the nucleic acids would include a variety of different six nucleotide fragments that consist of "a complement" of SEQ ID NO: 1. These claims are anticipated by the hexamar mix insofar as they require only a instant SEQ ID NO: 1 or "a complement thereof." The use of the indefinite article "a" to modify the required complement is interpreted to require that the claimed molecules only have to have any portion that is "a"

complement of SEQ ID NO: 1, including a single nucleotide. Amendment of the claim to require "the complement thereof" will overcome this rejection.

Response to Remarks

Applicant's remarks are addressed in the order they are set forth in their response.

Applicant's remarks regarding claim interpretation, namely (1) that the specification supports that SEQ ID NO: 1may encompass partial promoter sequences and (2) that regulatory elements can be found within intron regions of a gene are acknowledged. These possibilities have been considered.

Applicant traverses the rejection for lack of utility.

Applicant first argues out that claims 3, 5-7 and 9-10 are directed to transformed plant cells and plants and that these have utility independent of the function of SEQ ID NO: 1. However, the potential utilities set forth (for use in breeding programs, for example) are non-specific to the claimed invention as they could reasonably be applied to any possible plant cell or plant.

Applicant further argues that as the specification teaches that SEQ ID NO: 1 can be used as a regulatory region or a promoter (beginning at p. 9 of remarks). This potential use is discussed in the rejection, and as noted in the rejection it is not a substantial utility since the specification teaches with equal force that this same molecule also might be comprise regulatory elements (p. 16), may comprise genes encoding polypeptides or fragments thereof (p. 24) or may comprise introns and/or intron/exon junctions (p. 29). Instant SEQ ID NO: 1 cannot at the same time cannot encode a polypeptide and be a promoter or regulatory region, yet the specification

provides no guidance as to how to determine which of these may be applied to instant SEQ ID NO: 1. This deficiency in the specification is discussed in the rejection. Applicant's arguments do not address the contradictory nature of the specification, and thus the argument is not persuasive. Applicant argues at page 11 of the remarks that the Examiner has provided no support for the proposition that simply because SEQ ID NO: 1 is disclosed as having a promoter region or a partial promoter region does not necessarily exclude SEQ ID NO: 1 as also containing sequences encoding structural genes and comprising intron/exon boundaries. While it is within the realm of all possible things that this may be the case, the relatively short nature of SEQ ID NO: 1 suggests that it does not comprise all of a promoter, partial promoter, structural gene, intron and intron/exon boundary. Even if it does, applicant has not specifically taught in the specification that this particular molecule definitively has any of these portions, or if it does, how they function or what they encode. Applicant provided only general statements referring to over twenty thousand different molecules and no specific guidance regarding SEQ ID NO: 1. For the reasons of record, the rejection is MAINTAINED.

Applicant traverses the enablement rejection beginning on page 14 of the response.

Applicant argues that the use of the recited sequence within an expression construct would fall under the category of "conventional and well-known genetic engineering techniques." However, this is not persuasive. Indeed, inserting SEQ ID NO: 1 into a vector would be routine, but how SEQ ID NO: 1 might function once it is in the vector is entirely unpredictable. Since SEQ ID NO: 1 is disclosed as possibly containing one or all of a promoter, a partial promoter, a coding sequence, any sort of regulatory element or an intron or intron/exon boundary, one would have to undertake extensive experimentation to determine how and where to place SEQ

ID NO: 1 within a vector to accomplish the production of a construct that would function to cause the production of mRNA since as note in the rejection the order of elements within a vector is critical to the functioning of the vector. For example, if SEQ ID NO: 1 only contains a partial promoter sequence, the location of that partial promoter sequence within SEQ ID NO: 1 would have to be determined, and what is missing from that partial promoter sequence that would be necessary for driving promotion would have to be experimentally determined. The specification does not provide any guidance as to which portion of SEQ ID NO: 1 might be a promoter sequence or a partial promoter sequence or an enhancer. These constructs are not immediately evident simply by looking at the primary sequence, especially since one must also consider that SEQ ID NO: 1 might also include some structural coding sequence as well as a possible intron/exon boundary and other possible nucleic acid functions. Thus, the characterization that using SEQ ID NO: 1 within a promoter construct is "conventional and well-known" is misplaced, since it is neither conventional nor known what type of functional structures are actually comprised within SEQ ID NO: 1 or where they are comprised within the entirety of SEQ ID NO: 1. Applicant argues that this cannot be considered undue experimentation even if it is laborious, citing In re Angstadt. However, in the instant case, unlike the cited case, not a single working example of a construct which comprises SEQ ID NO: 1 within a promoter that functions as set forth in the claims or any other enabled utility for SEQ ID NO: 1 is provided. The instant situation differs tremendously from In re Angstadt, wherein a large number (forty) examples were provided, only one of which did not work. In In re Angstadt, the court determined that there was sufficient guidance in an unpredictable art. The court further stated, however, that "each case must be determined by its own facts." The facts of

this case do not support an enabled use for the claims, for all of the reasons discussed in the rejection. Applicant points to portions of the specification as providing guidance in the specification. These are addressed in the rejection, as is their insufficiency. Applicant further argues that practitioners in this art are guided by considerable knowledge and resources (p. 16), however this cannot overcome the fact that the specification does not clearly set forth which portions of SEQ ID NO: 1 comprise which of the many possible functionalities suggested by the specification. Regarding the unpredictability of the art, applicant argues that the references suggest modification can be made to promoter sequences. First, the instant case differs from the references because in the references it was known which portion of the starting material were promoter sequences. In this case, though the specification asserts that the SEQ ID NO: 1 might contain a promoter or partial promoter, it does not teach where within the sequence. For example, if SEQ ID NO: 1 contains a partial promoter as well as a coding gene, which comes first? The specificiation is silent. If SEQ ID NO: 1 contains a partial promoter, does that partial promoter function on its own, or does it need additional sequence to be included adjacent to it to function? If it needs sequence, what elements are missing? Even when the promoter portion of a nucleic acid has been identified, there was no way to predict which changes could be made to the sequence without abolishing function. Claims 12-15 allow for the modification of tens to hundreds of different nucleotides within SEQ ID NO: 1. There is no way to predict how one could change hundreds of nucleotides within SEQ ID NO: 1 and still arrive at a molecule that has any similar function to SEQ ID NO: 1, whether it be partial promoter function or enhancer function or encoding structural gene function. The rejection is maintained.

The written description and enablement rejections are WITHDRAWN, the first in view of applicant's remarks and the second in view of the amendments to the claims.

Conclusion

11. No claim is allowed.

12. **THIS** ACTION **IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Switzer whose telephone number is (571) 272-0753. The examiner can normally be reached on Monday, Tuesday or Thursday, from 9:00 AM until 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached by calling (571) 272-0745.

The fax phone numbers for the organization where this application or proceeding is assigned are (571) 273-8300. Any inquiry of a general nature or relating to the status of this

application or proceeding should be directed to the receptionist whose telephone number is (571)272-0507.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Juliet C. Switzer
Primary Examiner
Art Unit 1634

September 12, 2006

This is a result from a sequence search showing instant SEQ ID NO: 1 aligned to a gene encoding a P. coccineus putative POL3-like protein. The gene is listed in GenBank as accession AF325187. Below is a portion of the text of the record, followed by the alignment. In the alignment, instant SEQ ID NO: 1 is the top line (Qy) and the prior art gene is the bottom line (Db). The text of the record teaches that the mRNA includes nucleotides 28-595, 758-837 and 1270-1653 of the sequence (see bold portion of the "FEATURES" section). Instant SEQ ID NO: 1 aligns with the complement of nucleotides 1216-1553 of the record, which is a portion within the portion that makes up the coding sequence (i.e. the mRNA).

```
 AF325187/c
LOCUS       AF325187               4921 bp    DNA     linear   PLN 05-DEC-2001
DEFINITION  Phaseolus coccineus putative POL3-like reverse transcriptase
            (POL3-like) and suspensor-specific protein (G564) genes, complete
            cds.
ACCESSION   AF325187

FEATURES             Location/Qualifiers
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  Query Match             40.5%;  Score 159.4;  DB 8;  Length 4921;
  Best Local Similarity   66.9%;  Pred. No. 2.3e-34;
  Matches  226;  Conservative    0;  Mismatches  112;  Indels    0;  Gaps    0;

Qy          1 AGCTTTCCCTCTTTGAACAAATACCCCTCAGCCAAATAGAATCCATCTTGGGCCTTTTTC 60
              || ||||| ||||| || | ||| ||||| | || |||| | ||  |||| ||  | |
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Qy         61 CCACAACTCTCATAAATGGGAGAGAAATGTTCATCTAAAGCATACAAGTCCCTAATATTA 120
              |||     |||| |||| ||||  | || ||||     ||| |  || || || |
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Qy        121 TCAAATCCTAAAATTTGAGCTCCTAGGGAGCAAAACAATGTGTGTCTCCTAGAGAGGGCA 180
              |||||||| | |||||| || |||||     |||| |  ||||| |  ||||| || |||
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Qy        181 TCAGCTACCACATTTGTTTTTCCCTTTTTGTATTTGATAACATATGGAAATTGCTCTAGG 240
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